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BRAIN activation of 11 healthy right-handed subjects was studied with magnetoencephalography to estimate individual hemispheric dominance for speech sounds. The auditory stimuli comprised binaurally presented Finnish vowels, tones, and piano notes in groups of two or four stimuli. The subjects were required to detect whether the first and the last item in a group were the same. In the left hemisphere, vowels evoked significantly stronger (37–79%) responses than notes and tones, whereas in the right hemisphere the responses to different stimuli did not differ significantly. Specifically, in the two-stimulus task, all 11 subjects showed left-hemisphere dominance in the vowel *vs* tone comparison. This simple paradigm may be helpful in non-invasive evaluation of language lateralization. *NeuroReport* 10:2987–2991 © 1999 Lippincott Williams & Wilkins.

Key words: Healthy subjects; Hemispheric dominance; MEG; Speech sounds; Vowels

Left-hemisphere dominance for processing of vowels: a whole-scalp neuromagnetic study

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Introduction

The left and right hemispheres of the brain are not symmetrically involved in language processing. Clinical observations and neuropsychological studies suggest that while the great majority of right-handed individuals show a left-hemisphere dominance for language, a minority of them are right-hemisphere dominant [1,2].

Knowledge about language lateralization is of special value in evaluation of patients who are candidates for brain surgery (e.g. removal of an epileptic focus or a brain tumor from the temporal lobe). Since resection of brain regions that contribute to basic language skills is likely to result in language impairments, it is essential to determine preoperatively which hemisphere is dominant for language. Traditionally, language dominance is determined with the Wada test [3]. This technique involves intracarotid application of amobarbital, allowing selective inactivation of one hemisphere at a time. Because of the health risks involved, attempts have been made to find non-invasive methods. In recent years, developments in neuroimaging techniques have provided new tools for studying language dominance. One of these techniques is magnetoencephalography (MEG), measurement of the neuromagnetic field outside the head to probe neural electric activity of the brain. Previous MEG work has indicated that it is possible to use MEG to examine hemispheric differences for language processing at an individual level [4,5].

The purpose of the present study was to develop a simple task that might be useful for presurgical evaluation of language lateralization. As the first step, we examined neuromagnetic responses associated with attentive processing of vowels, tones, and piano notes in both hemispheres of healthy subjects. The results imply left hemisphere dominance for processing of vowels. In future, this approach might provide a new tool for evaluation of individual hemispheric dominance for language.

Materials and Methods

Subjects: Eleven healthy subjects (23–30 years, mean 27.1; four females and seven males) were studied. All were native Finnish speakers. Hand preference was evaluated with the Edinburgh Inventory [6]. Possible outcomes of this inventory are between +1.0 (strongly right-handed) and –1.0 (strongly left-handed). In the present study, all subjects were right-handed and had a minimum score of +0.7.

Stimuli and task: Within one session, the subjects listened to three types of digitally recorded auditory stimuli: Finnish vowels, tones, and piano notes (see Fig. 1). Frequencies of the tones and the fundamental frequencies of the notes were 394, 442, 496, 525 and 589 Hz which equal G, A, B, C, and D on a tempered scale. A native speaker of Finnish pronounced the vowels (A, E, U, I, O). All sounds were of equal duration (250 ms); the tones and notes also

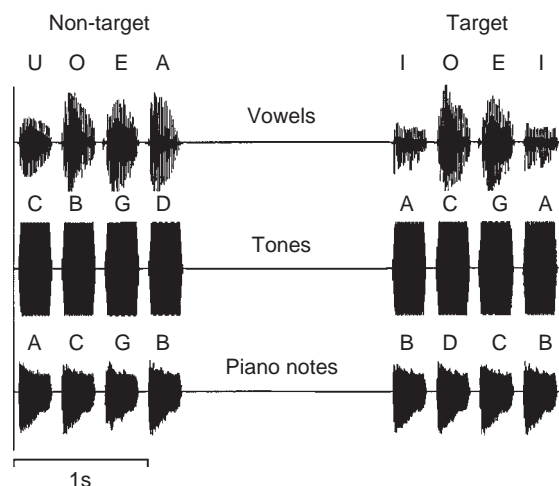


FIG. 1. Examples of the three types of auditory stimuli used in the four-sound task: vowels, tones and piano notes.

included 20 ms rise and fall times. Stimuli were presented binaurally with the stimulus intensity adjusted to a comfortable listening level.

In the two-sound task, pairs of vowels, tones, and notes were presented. The silent interval between the two stimuli of a pair was 70 ms, and the interpair interval was 1590 ms. The subject had to respond by lifting the left index finger when the two sounds of the pair were identical (target). No response was required when the two sounds differed (non-target). The four-sound task consisted of trains of four vowels, tones, and notes. Again the sounds within a trial were separated by 70 ms and the intertrain interval was 1590 ms. In target trains, the first and the fourth stimuli were identical while they differed from each other in the non-target trains. In both target and non-target trains, the second and third items were different from each other and from all other items. In both tasks, targets (20%) and non-targets (80%) of all three types were presented in a pseudo-random order: two targets and two similar pairs or trains in a row were not allowed. To ascertain that the subjects understood the instructions completely, feedback about individual performance was given during a short practice trial. The subjects were instructed to avoid head movements and eye blinks.

Recording: MEG signals were recorded in a magnetically shielded room, using a 306-channel whole-scalp neuromagnetometer (Vectorview, Neuromag Ltd). The instrument has 102 recording sites which contain planar gradiometers measuring the longitudinal and latitudinal derivatives of the magnetic field normal to the magnetometer helmet ($\partial B_z/\partial x$) and ($\partial B_z/\partial y$) (204 in total) and magnetometers (102 in

total). The signals were bandpass filtered at 0.03–200 Hz and digitized at 600 Hz. Responses to the different stimulus categories were averaged online over a 2300 ms interval in the two-sound task and a 2500 ms interval in the four-sound task, both including a 200 ms prestimulus baseline. About 100 responses to the non-target pairs/trains were collected for the three stimulus categories. Epochs contaminated by eye movements and blinks (monitored with electro-oculogram) were discarded from averaging. For subsequent analysis, the averaged responses were low-pass filtered at 40 Hz (roll-off width 10 Hz). A 200 ms prestimulus baseline was used for amplitude measurements.

Analysis: Only responses to non-target stimuli were analysed in detail. In signal analysis we only took into account the planar gradiometers. By calculating the vector sums of the longitudinal and latitudinal derivatives of the responses, $\text{SQRT}((\partial B_z/\partial x)^2 + (\partial B_z/\partial y)^2)$, information about direction of neural currents was omitted in favour of information about the strength of the response.

Two time intervals were set for further analysis: interval A, ± 25 ms around the peak of the 100 ms response (N100m) to the onset of the first sound and interval B, from onset of the second sound until 320 ms after the onset of the last sound (320–640 ms in the two-sound task and 320–1280 ms in the four-sound task). For each individual and each time interval, we selected over the temporal lobe of each hemisphere the gradiometer pair which showed the highest peak amplitude to vowel stimuli. We then calculated the mean activation at this channel pair for both time windows. The amplitudes were normalized according to each individual's left-hemisphere response to vowels. A two-tailed *t*-test was used in statistical evaluation of the group data. We also calculated a laterality index (LI) for each subject according to the formula $(L-R)/(L+R)$, where L and R refer to the ratios of response amplitudes to vowels *vs* tones or notes, in the left and right hemispheres, respectively.

Results

Behavioural measures: In the two-sound task, subjects performed equally well in trials involving tones, piano notes and vowels. However, in the four-sound task, subjects tended to perform worse for tones and notes than vowels (binomial test, $p=0.06$).

Responses to different stimuli: All stimuli evoked strong N100m responses over the temporal areas about 100 ms after pair/train onset. Subsequent

peaks were observed ~100 ms after the onset of each sound in the sequence: around 420 ms in both tasks, and additionally around 740 ms and 1060 ms in the four-sound task.

Figure 2 displays vector sum responses in one subject over both temporal regions in the four-sound task. The responses are clearly stronger to vowels than to tones and notes over the left hemisphere, whereas no such difference is seen over the right hemisphere. A similar pattern was observed in most subjects. Four individuals showed stronger responses to vowels than to tones and notes over the right hemisphere as well, but the relative increase was smaller than over the left hemisphere. In the two-sound task, similar differences were found between the responses (data not shown).

Mean activation following different stimuli: Figure 3 shows mean amplitudes for the three stimulus

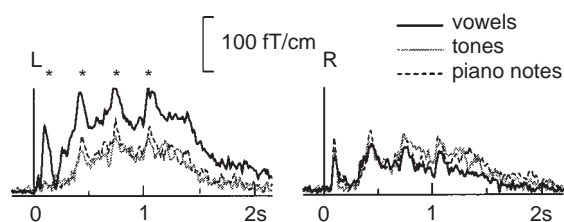


FIG. 2. Vector sums in one subject from sensors over the left (L) and the right (R) temporal regions which showed the highest amplitude to vowels between 320 and 1280 ms in the four-sound task (stars indicating peaks).

categories over both hemispheres, separately for the two tasks and time intervals. During interval A (± 25 ms around the first N100m peak) in the two-sound task, vowels evoked in the left hemisphere on average 70% and 72% stronger responses than notes and tones, respectively ($p < 0.001$). During interval A in the four-sound task, responses were on average 85% and 87% stronger to vowels than notes and tones, respectively ($p < 0.001$). In the right hemisphere, however, in both tasks, responses to tones, notes and vowel stimuli were not statistically significantly different.

During interval B in the two-sound task (320–640 ms), the left hemisphere responses to vowels were on average 61% and 39% stronger than responses to notes and tones, respectively ($p < 0.001$). During interval B in the four-sound task (320–1280 ms), the left hemisphere responses were on average 79% and 54% stronger to vowels than to notes and tones, respectively ($p < 0.001$). Again, in the right hemisphere, responses to the different stimuli did not differ statistically significantly in either task.

Hemispheric laterality in individual subjects: Figure 4 shows that, during interval A in the two-sound task, 10 out of 11 subjects (with the exception of S8) had a positive LI, indicating a stronger difference between responses to vowels *vs* tones and notes in the left than the right hemisphere. Individual LIs were approximately similar during interval

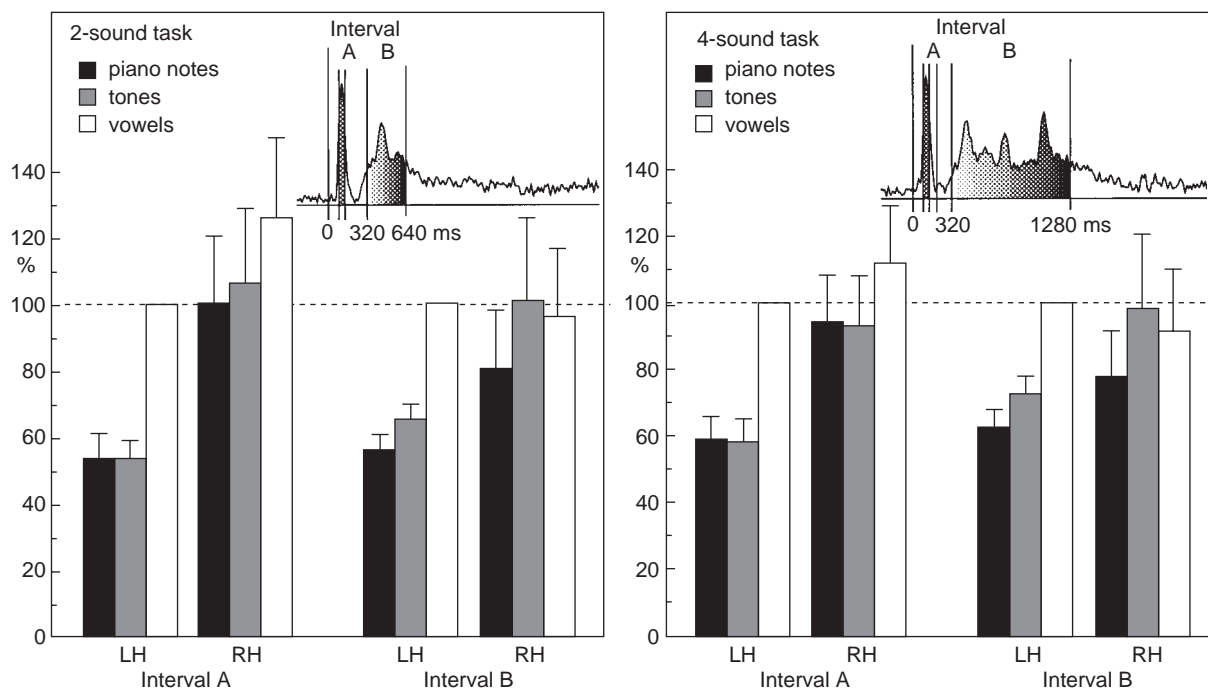


FIG. 3. Mean (\pm s.e.m.) amplitudes for the 11 subjects during both tasks and both time intervals. Amplitudes were normalized according to the individual left hemisphere response to vowels. LH, left hemisphere; RH, right hemisphere.

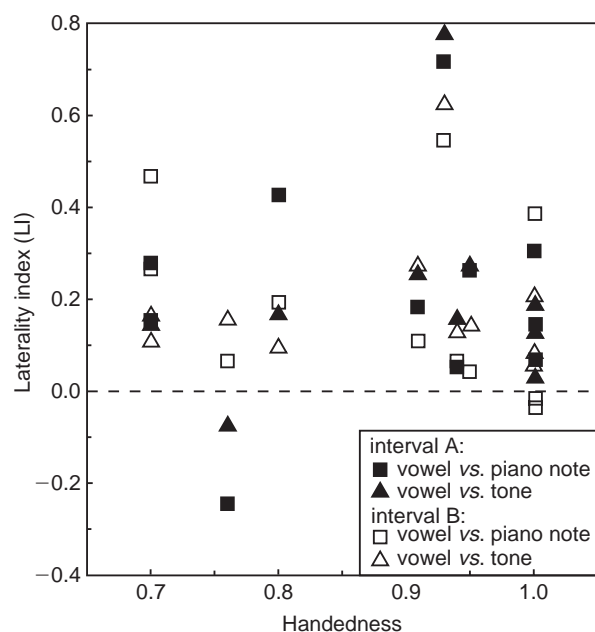


FIG. 4. Individual laterality indices during the two-sound task vs the right-handedness as measured by the Edinburgh Inventory.

A in the four-sound task (data not shown). During interval B in the two-sound task, all 11 subjects showed a positive LI for the vowel *vs* tone comparison but only nine (with the exception of subjects S6 and S10) for the vowel *vs* piano comparison. During interval B in the four-sound task, nine subjects (with the exception of S8 and S11) showed a positive LI for the vowel *vs* tone comparison (data not shown) and 10 for the vowel *vs* piano comparison (all except S9). Table 1 summarizes the results.

No relationship was observed between the degree of handedness and the degree of hemispheric dominance as determined by the laterality index (see Fig. 4).

Discussion

In the mean data across all 11 subjects, the responses were significantly stronger to vowels than to tones or piano notes over the left but not the right hemisphere, suggesting left-hemisphere dominance for processing of vowels. Similar differences were seen

both during the N100m response and during the later time window (320–640 ms in the two-sound task and 320–1280 ms in the four-sound task).

According to individual laterality indices, all subjects were left hemisphere dominant for the vowel *vs* tone comparison during 320–640 ms in the two-sound task. In the corresponding vowel *vs* piano comparison, and during other intervals in both tasks, left hemispheric dominance was obtained in nine or 10 out of the 11 subjects. In total five subjects showed inconsistent hemispheric dominance when both vowel *vs* tone and vowel *vs* piano comparisons in the later time intervals of both tasks were taken into account. Around the N100m peak, hemispheric dominance for speech sounds was consistent for individual subjects over both the vowel *vs* piano and vowel *vs* tone comparisons in both tasks.

In most experimental conditions, ten (91%) out of the 11 subjects showed indices favouring the left hemisphere. This number is consistent with results from Wada tests, indicating left hemisphere language dominance in 92–99% of right-handed subjects [1,3]. In previous MEG [4], PET [7], fMRI [7] and EEG [8,9] studies, 78–93% of right-handed subjects (sample sizes varying from nine to 28 subjects) have been considered left hemisphere dominant. Some subjects showed a vowel–tone difference also in the right hemisphere, suggesting bilateral representation of speech-related processing, although with left hemisphere dominance.

Our aim was to develop a straightforward clinical test for language dominance. Thus, we did not attempt to model the N100m responses, which are known to originate in the region of the supratemporal auditory cortex [10]. We rather compared the response strengths between stimuli within each hemisphere and the resulting ratios across hemispheres. Such a comparison was feasible with our planar gradiometers which detect the maximum signal immediately above the active cortical area [11]. The absolute signal amplitudes depend, besides the source strength, also on the distance of the detectors from the source, but as we used relative values, we did not need to take this issue into account. The differences were more clear between vowels *vs* tones than vowels *vs* notes, which will further simplify the future clinical tests.

Our task, in which the subjects had to judge whether the first and the last sound in a series were the same, kept the subject's vigilance stable but probably also involved short-term memory mechanisms. However, it is highly unlikely that the differences between responses to vowels *vs* other sounds would be memory-related because the effect was observed already around the N100m response to the first sound of the sequence.

Table 1. Percentage of subjects showing a positive laterality index (LI); the subjects with negative LIs are indicated within brackets. Data are given separately for vowel *vs* tones and vowel *vs* piano comparisons during intervals A and B in both tasks

Task	Interval	Vowel <i>vs</i> tones	Vowel <i>vs</i> notes
Two-sound	A	91% (S8)	91% (S8)
	B	100%	82% (S6, S10)
Four-sound	A	91% (S8)	91% (S8)
	B	82% (S8, S11)	91% (S9)

It is somewhat surprising that consistent hemispheric asymmetry for speech sound processing was reflected in the N100m response which can be elicited in any abrupt change in the auditory environment [10]. However, in line with our data, Poeppel *et al.* [5] have reported an effect in N100m specific to attentive discrimination of syllables. It is thus possible that the N100m response not only reflects acoustic but also phonetic aspects of the stimuli.

Eulitz *et al.* [12] found stronger left than right hemisphere responses to vowels than tones when the subjects made covert judgements about stimulus duration (short or long); similarly to our study, the difference between responses to vowels *vs* tones was larger over the left than the right hemisphere. However, hemispheric asymmetries were significant only at 400–600 ms but not during the N100m response.

Conclusion

Our results imply left hemisphere dominance for speech sound processing in right handed subjects,

both during the N100m response and at later latencies. The present task, simplified to vowel *vs* tone comparison only, might be helpful in non-invasive presurgical evaluation of language lateralization. A necessary future step is to compare this task and the results of Wada test at individual level.

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